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Current management of sepsis and septic shock

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ABSTRACT

Sepsis remains a leading cause of death in the intensive care unit. With no specific sepsis therapies available, management currently relies on infection control and hemodynamic stabilization. Rapid diagnosis enabling early initiation of appropriate therapy is essential to maximize survival rates. Effective antimicrobial therapy should be started as soon as possible after diagnosis, with empirical choices based on likely pathogens, local microbiological patterns, and any recent antimicrobial therapy. At the same time, fluids and vasopressor agents should be commenced to restore and maintain hemodynamic stability and adequate tissue perfusion. No effective immunomodulatory therapies are available, but some candidates are undergoing clinical trials. Better techniques for characterization of the degree of sepsis response in individual patients are needed to help target such agents more appropriately as some patients may benefit from immunosuppressive agents while others may require an immune stimulating intervention. The management of patients with septic shock is often complex and the development of sepsis teams should be encouraged so that the multiple components of treatment, e.g., insertion of intravascular lines, blood sampling for culture and biochemistry, positioning of required monitoring devices, fluid, antibiotic and vasoactive drug administration, etc, can be carried out simultaneously.

Key words: infection, fluid resuscitation, immunomodulation, organ dysfunction, sepsis team, vasopressors

INTRODUCTION

Sepsis is defined as "life-threatening organ dysfunction caused by a dysregulated host response to infection" (1) and septic shock as sepsis with persistent arterial hypotension requiring vasopressor support despite adequate fluid resuscitation and presence of perfusion abnormalities, such as oliguria, reduced peripheral perfusion, and altered mental status. Patients with septic shock also have hyperlactatemia (blood lactate concentrations > 2 mEq/L). Hospital mortality rates for patients with septic shock remain > 40% (1, 2) despite some reduction in recent years as a result of improvements in general patient management.

IMPORTANCE OF EARLY TREATMENT

One of the key aspects of patient management is early recognition of sepsis so that antibiotics and other interventions can be started rapidly before organ dysfunction worsens. Early appropriate management has been demonstrated in several studies to be associated with improved outcomes (3, 4) and awareness of sepsis as a possible diagnosis is, therefore, crucial. However, diagnosis of sepsis can be difficult, especially in critically ill patients in whom many of the typical signs and symptoms present in sepsis, e.g., fever, tachycardia, tachypnea, raised white cell count, can also be due to other acute conditions. Nevertheless the presence of several of these signs should alert the attending physician to the possibility of a diagnosis of infection and spur further relevant investigations to identify a possible source. Importantly too, absence of these signs does not mean that sepsis can be ruled out; indeed, hypothermia and leukopenia may equally be present in patients with sepsis and are associated with a worse prognosis. Sepsis is more commonly recognized by the associated organ dysfunction. The recently proposed qSOFA (quick sequential organ failure assessment) score (1) can be used, particularly on the general ward, to identify some degree of organ dysfunction that may be an expression of sepsis. The presence of raised biomarker levels, e.g., C-reactive protein (CRP) and/or procalcitonin (PCT), although also non-specific, can indicate a likely diagnosis of sepsis in combination with clinical signs and symptoms. (5) As culture results are often negative in critically ill patients (6, 7), largely due to recent or ongoing antimicrobial therapy, identification of infection is also complicated. Sepsis is, therefore, more often diagnosed as a result of unexplained organ dysfunction, leading to a search for an underlying cause, than from the presence of diagnosed infection. (5)

KEY ASPECTS OF MANAGEMENT

The management of sepsis essentially relies on treatment of the underlying source of infection and support of failing organs. No specific immunomodulating therapies are currently available although considerable research is ongoing in this field.

TREATMENT OF INFECTION

The source of infection must be removed as soon as possible. This may require sur-

gical drainage of an abscess or removal of infected intravenous or arterial lines or catheters. If no source is obvious, further clinical and microbiological examinations and imaging should be conducted to try and locate one, focusing initially on the most likely culprits, i.e., the lungs, abdomen, urine, wounds, and indwelling devices. Appropriate antibiotics at correct doses should be initiated as soon as possible (8, 9) with empirical choices based on likely pathogens, local microbiological patterns, and any recent antimicrobial therapy. If possible all relevant cultures should be taken before antibiotics are started but not if this delays a life-saving antibiotic treatment (the typical example being meningococcemia). Once culture results are available, antibiotics can be adapted accordingly. Sometimes the spectrum should be enlarged to cover for additional organisms or resistances. More often these results can allow the spectrum of coverage to be reduced according to the identified organisms and susceptibilities. However, this approach may not be possible in all patients (7), either because cultures remain negative or because the cultures grow multiple organisms (e.g., in severe intraabdominal infections).

In general a 7- 8-day course of antibiotics is sufficient in most ICU patients and shorter courses may suffice in some patients with good source control. Biomarkers, notably procalcitonin, have been suggested as possible aids to guide antimicrobial therapy (10), but they should not be used in isolation. Clearly, decisions when to stop antibiotic therapy need to be made on an individual patient basis taking all available clinical, laboratory and microbiological data into consideration. (9)

HEMODYNAMIC SUPPORT

Hemodynamic support essentially consists of fluids and vasoactive agents. If septic shock is present, fluid administration should be considered in four phases according to the SOSD (Salvage, Optimization, Stabilization, De-escalation) mnemonic. (11) In the early salvage phase, fluids should be given liberally at 20 to 30 ml/kg. Once the patient is out of immediate danger, fluid administration should be titrated according to patient needs, assessed using repeated fluid challenges. (12) During this optimization phase, patients should be monitored closely to limit adverse effects of excess fluid including pulmonary edema. Fluid challenges must be carefully conducted using the TROL concept to remember the four components: T (type of fluid); R (rate: 150-300 mL over 10 mins); O (objective, e.g., arterial pressure or heart rate); and L (limits, e.g., pre-fixed central venous pressure level) (13). Importantly no other interventions should be performed during a fluid challenge. Other dynamic measures, e.g., or pulse pressure or stroke volume variation, or echocardiographic evaluation of the size of the vena cava can be used to evaluate likely response to fluids, but all have their limitations. (14) Passive leg raising is a relatively complex procedure requiring close stroke volume monitoring. Hence, fluid challenges remain the most reliable approach. Once the shock episode is resolved, and the patient is stable, fluid intake should be reduced to provide just maintenance with replacement of ongoing losses. Finally, once the patient is recovering, excess fluid is removed as positive fluid balances have been associated with worse outcomes. (15) In many patients, spontaneous diuresis will be sufficient but some patients may require renal replacement therapy for ultrafiltration. The choice of fluid has been widely debated and remains uncertain as all have adverse effects. Crystalloid fluids are generally used as first-choice fluids with addition of a colloid, e.g. albumin, when large amounts of crystalloids are required. Hydroxyethyl starch (HES) solutions are no longer recommended in sepsis.

Vasopressor agents should be started at the same time as fluid resuscitation to help restore perfusion pressure early. (16, 17) Norepinephrine is the vasopressor of choice (18, 19). Low doses of dobutamine (about 5 mcg/kg/min) may be used simultaneously to increase cardiac output and oxygen delivery to the tissues.

IMMUNOMODULATION

No effective immunomodulatory therapies are currently available. Techniques that allow for a better characterization of the degree of sepsis response in individual patients may facilitate future development of specific agents as some patients may benefit from immunosuppressive agents while other may do better with an immune stimulating intervention. The optimal type of therapy may vary in the same patient over time.

Moderate doses of corticosteroids are sometimes used in patients with severe septic shock, but this is not universally accepted. (20)

THE TEAM APPROACH

A diagnosis of sepsis requires that the patient is urgently taken in hand by a physician specialized in sepsis management. Management can be optimized by the presence of a sepsis team, comprising nurses, intensivists, a phlebotomist, an infusionist, a microbiologist, a radiographer, a surgeon, etc. The precise composition will of course depend on local resources, hospital organization, and availability and may vary according to the type of patient. In this way, various aspects of management insertion of intravenous/arterial lines, blood sampling for laboratory and culture, fluid and antibiotic administration, positioning of monitoring equipment, vasoactive agent administration, etc can be delegated appropriately and performed simultaneously thus saving time. One team leader will oversee the process and check that nothing has been forgotten. Many hospitals now have special sepsis teams and studies have demonstrated that this approach can improve patient outcomes. (21)

CONCLUSION

Awareness of sepsis as a possible diagnosis will help earlier identification of at risk patients, in turn facilitating more rapid intervention. Effective source removal and antibiotic treatment and adequate hemodynamic support remain the cornerstones of treatment for these patients. Other organ dysfunctions must be managed as they arise with appropriate organ support and general aspects of patient management such as those included in the FAST-HUG mnemonic (22) must also be remembered (Figure 1). All treatments must be adapted to individual patient characteristics. Use of dedicated sepsis teams will help to ensure that patients receive the early management they require.

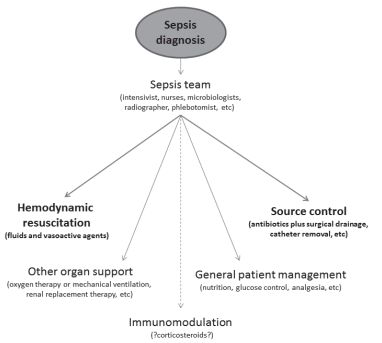

Figure 1. The key components in the management of the patient with sepsis

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